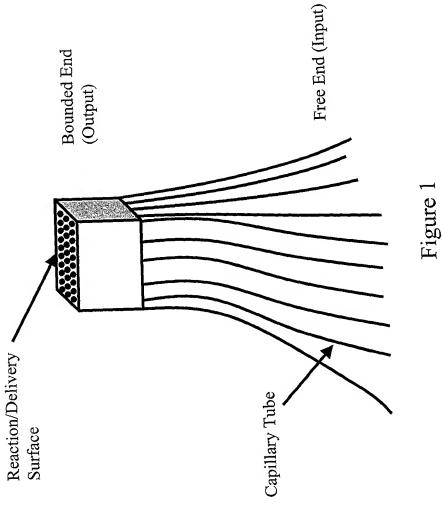
Sheet 1 of 58 Title: METHOD AND APPARATUS BASED ON BUNDLED CAPILLARIES
TOR HIGH THROUGHPUT SCREENING
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Application 140:: 10/080,274

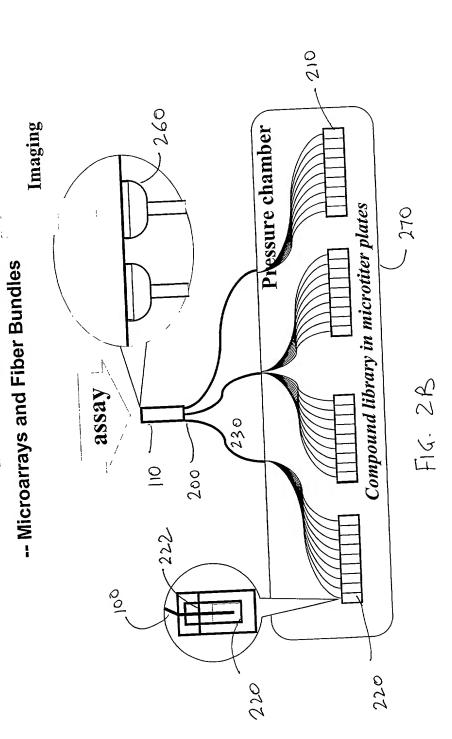
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Compressed air 220 enclosure 270 Chemical Compound 222 Capillary Take 100

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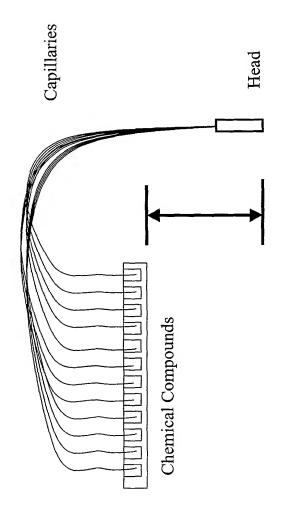




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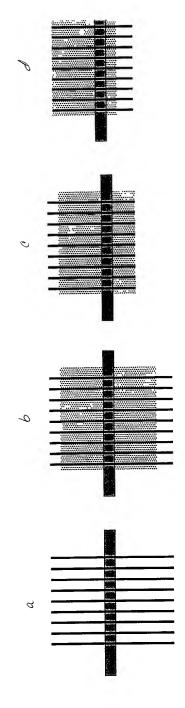


Fig. 4. Fabrication of delivery head using a guide plate

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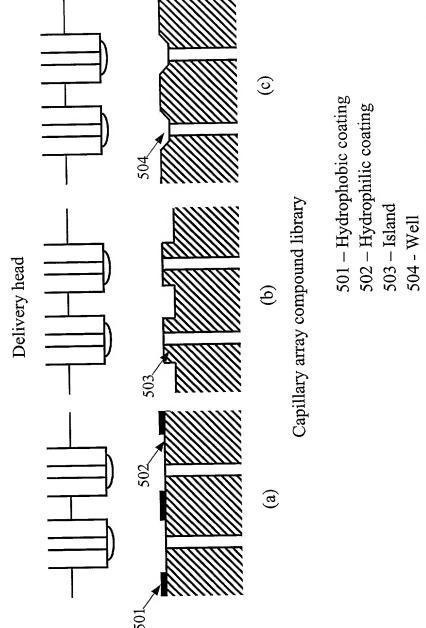


Fig. 5. Surface features on the surface of the capillary array compound library to prevent crosscontamination during compound loading

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surface Assay

Top View

Side View

Fig. 6. Basic configuration of capillary array substrate for the portable compound library Title: METHOD AND APPARATUS BASED ON BUNDLED CAPILLARIES FOR HIGH THROUGHPUT SCREENING Inventor: Jianming XIAO et al. Application No.: 10/080,274 Docket No.: 473532000620

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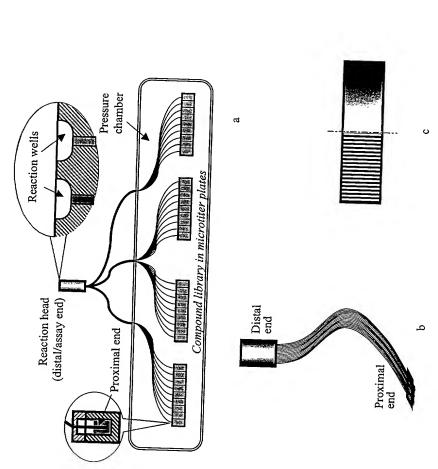
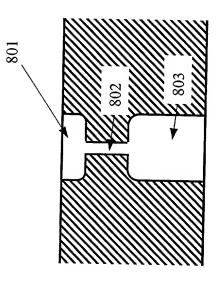


Fig. 7 The capillary array compound library in different formats



801 – Mixing/reaction well 802 – Flow regulator for reagent metering 803 – Compound reservoir

Fig. 8. Internal structure of a through hole in capillary array compound library

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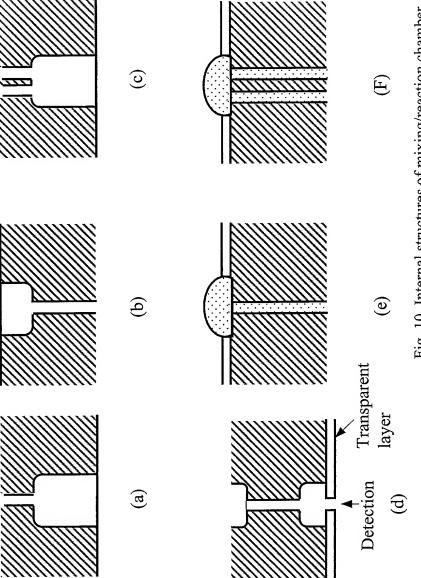


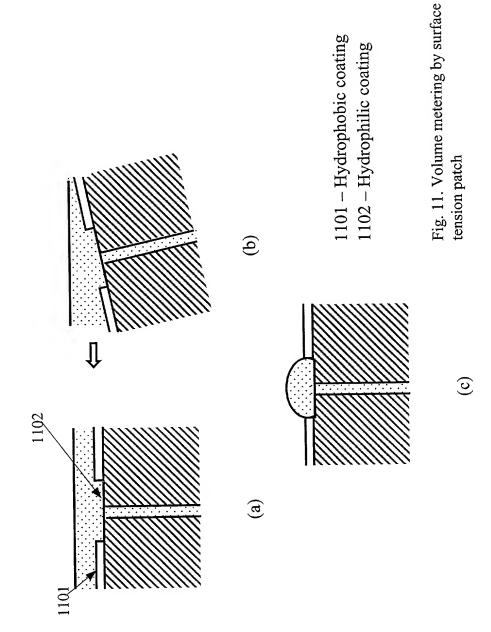
Fig. 10. Internal structures of mixing/reaction chamber

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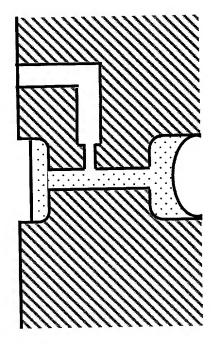
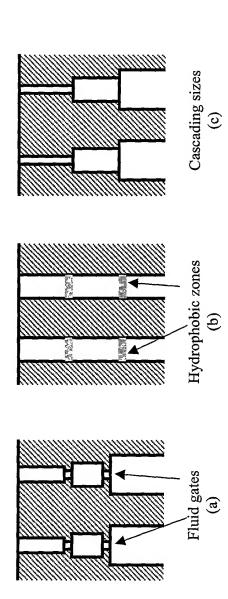


Fig. 12. Fluid regulator with side air tunnel

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Fig. 13 Internal through hole structures to facilitate chamber volume metering and mixing



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Fig. 14 Process of metering multiple reagents using interconnected chambers

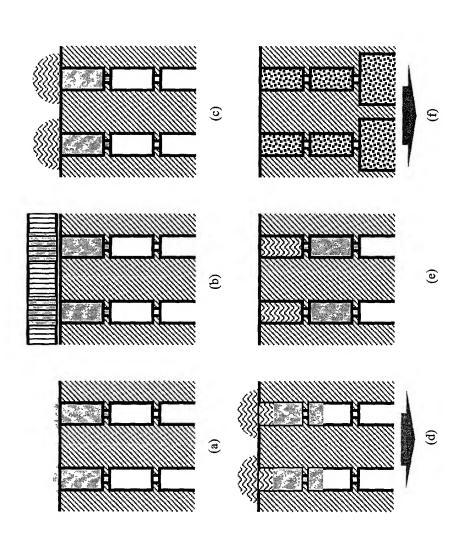
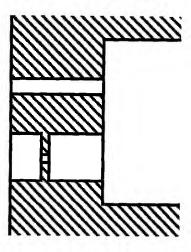


Fig. 15 Special through hole structure where multiple chambers links to a chamber in parallel



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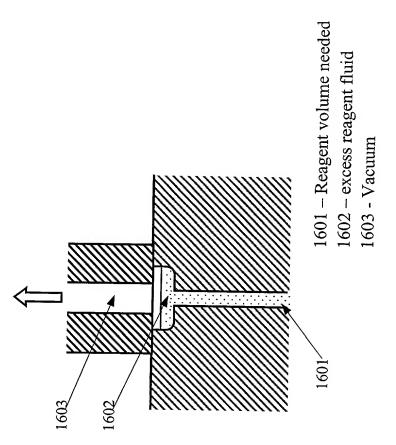


Fig.16. Removal of excess fluid by vacuum

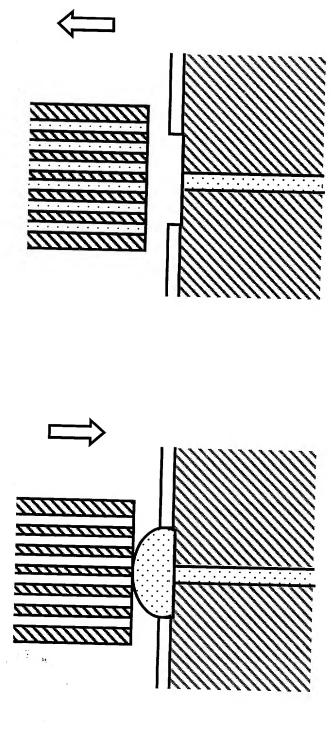


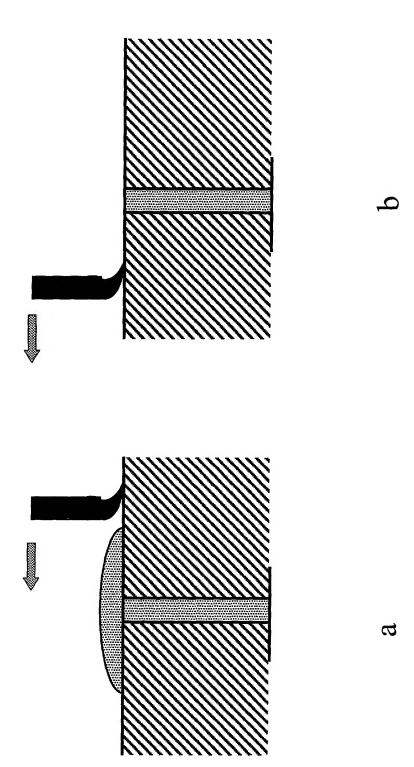
Fig. 17. Excess fluid removal using a second capillary array

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Fig. 18. Excess Fluid Removal by Wiping



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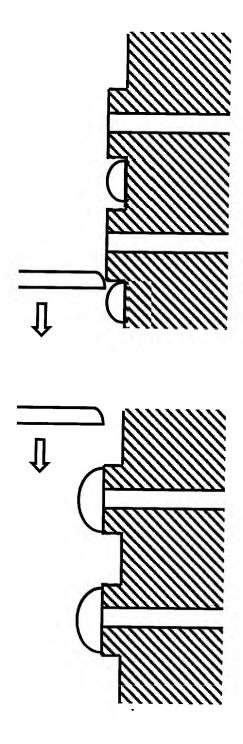
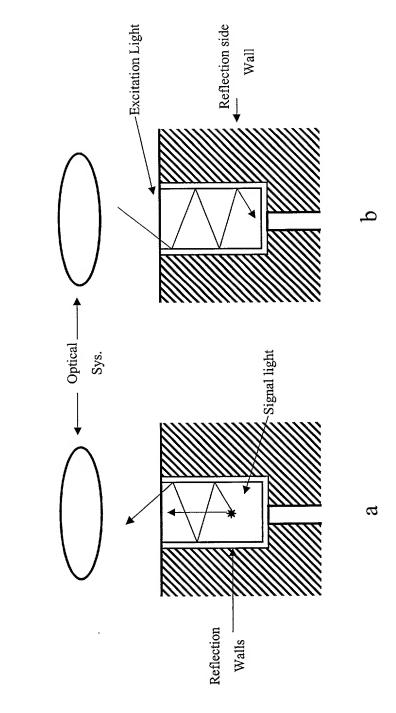


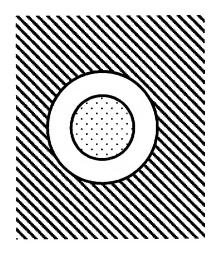
Fig.19. A method for reducing cross-contamination between adjacent holes during excess fluid removal

Fig. 20. Using Reflection Wall of Reaction Chamber to Enhance Optical Signal of the Assay



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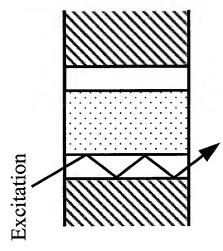


Fig 21. Light guiding capillary

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other blocking options to be tested:

FIG 22B

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-NO₂ (EtO)₃SiH Si(OEt) 3 solution phase silanization O₂N O₂N´ UV-light 350nm O₂N O₂N O₂N

FIG ZZC

Process for fabrication using a negative Figure 23

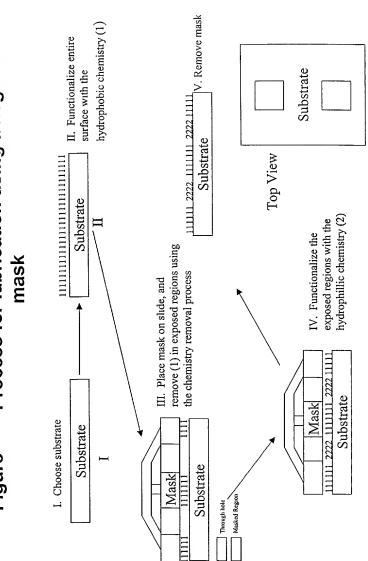
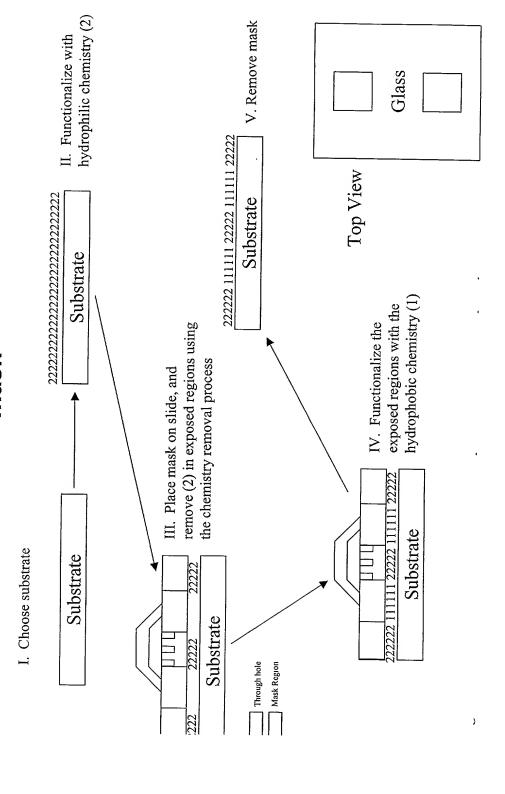
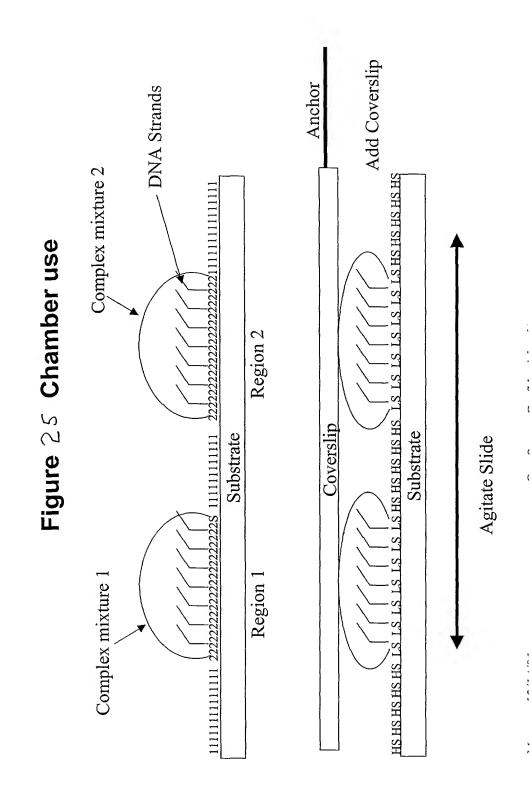


Figure 24 Process for the fabrication using positive mask



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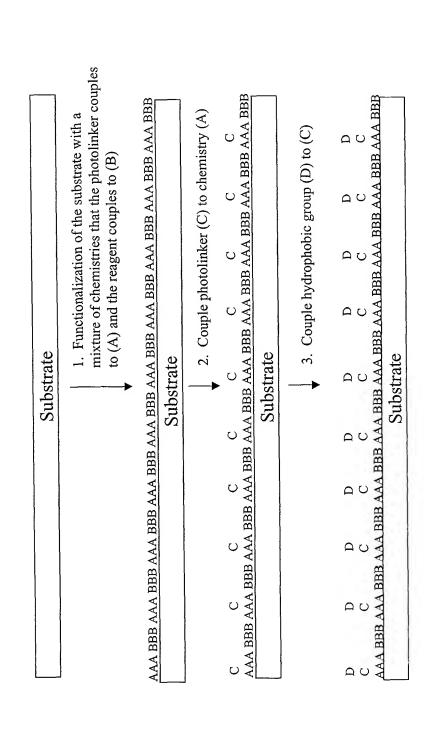
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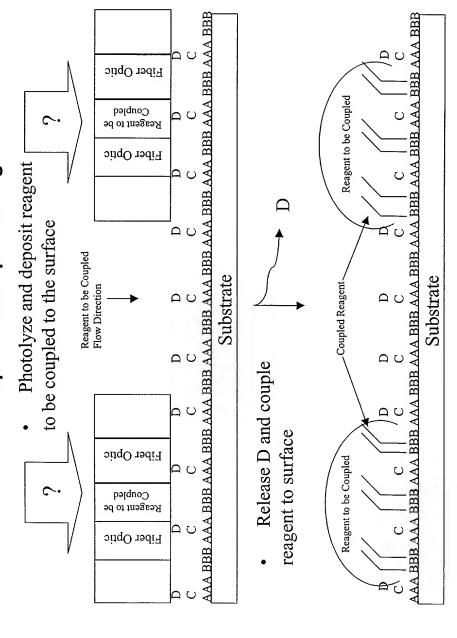
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Figure 264 Surface Tension Patterning: On-capillary Fiber optic based patterning



Surface Tension Patterning: On-capillary Fiber optic based patterning Figure 2 6B



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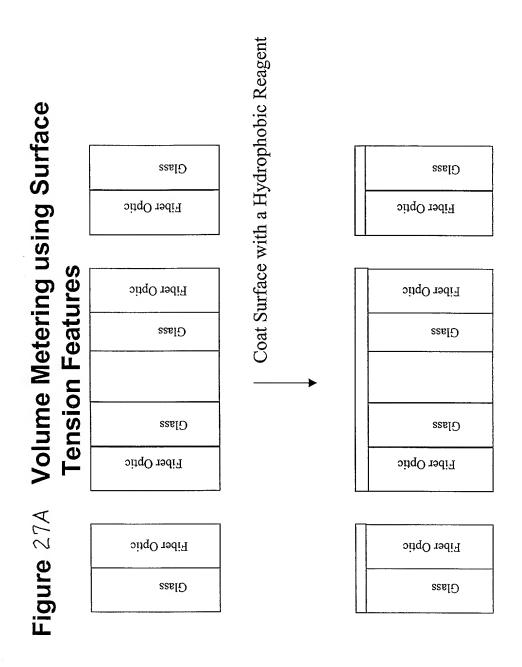
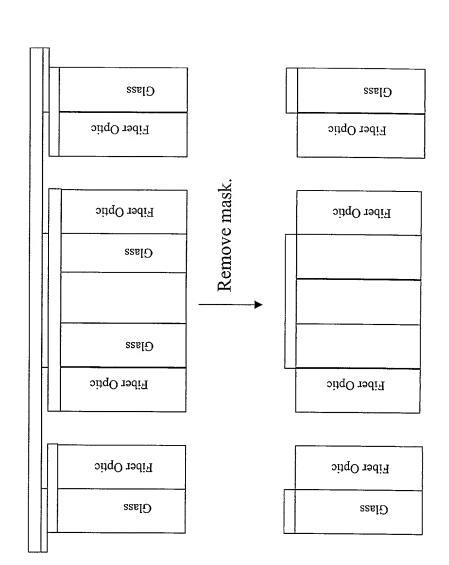


Figure 27B Volume Metering using Surface Tension Features

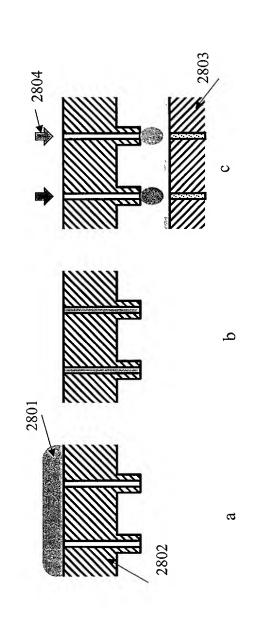
Place a Mask on to the Surface and Expose the Surface to the Chemistry Removal Process



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Fig. 28 Reagent pre-metering using an intermediary through-hole array



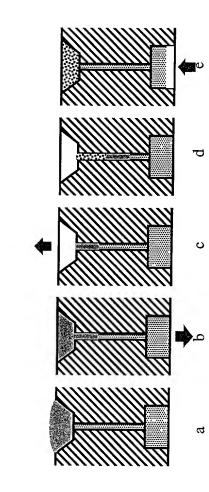
2801 - reagent fluid applied in excessive;

2804 - pressure

^{2802 -} intermediary through hole array;

^{2803 -} capillary array compound library;

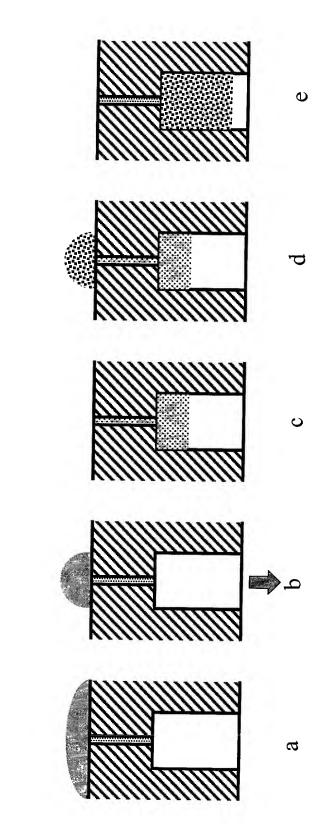
Fig. 29 Metering and mixing with a multi-use capillary array compound library



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Fig. 30 Metering with hydrophilic patch and mixing

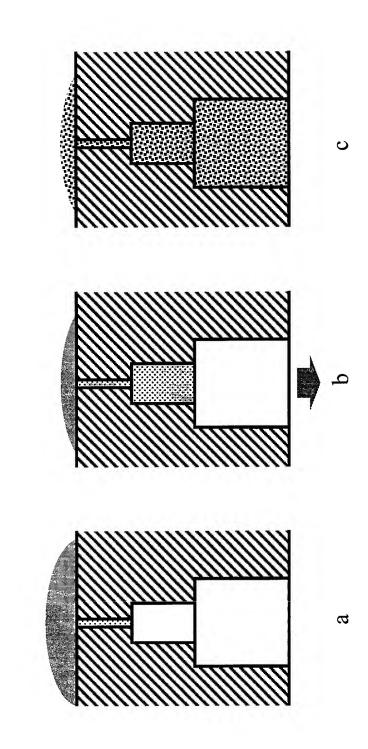


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Fig. 31 Mixing and metering with interconnected chambers



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 σ Fig. 32 Heterogeneous Assay ದಿ Target Probe B mixture ಡ ð Probe A

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Antibody Immobilization via the Carbohydrate Moiety

1. Oxidation of antibodies vicinal diol group to its aldehyde

2. Conjugation of maleimide moiety with antibody

3. Immobilization of the modified antibody to the surface.

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Immobilization via Amine Goups

1. Hydrosilylation of (3-mercaptopropyl)triethoxysilane on the surface of fiber

2. Formation of a thioether bond

· 3. Attachment of fiber to antibody

Antibody Immobilization via Streptavidin

1. Label antibody with biotin

2. Modification of fiber surface with biotin maleimide

Meeting 12/14/01

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Antibody Immobilization via Streptavidin

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3. Conjugate Streptavidin to the surface

4. Conjugate Biotin Anitbody to the surface

Formation of thiazolidine

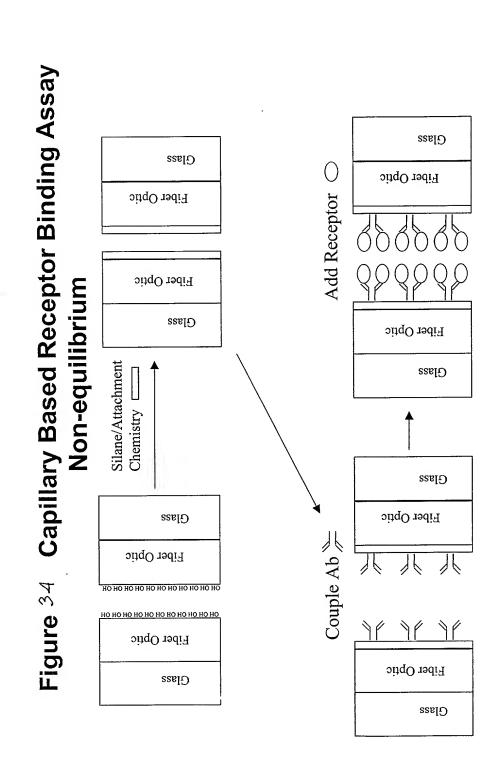
1. Surface attachment and formation of the linker

2. Thiazolidine formation

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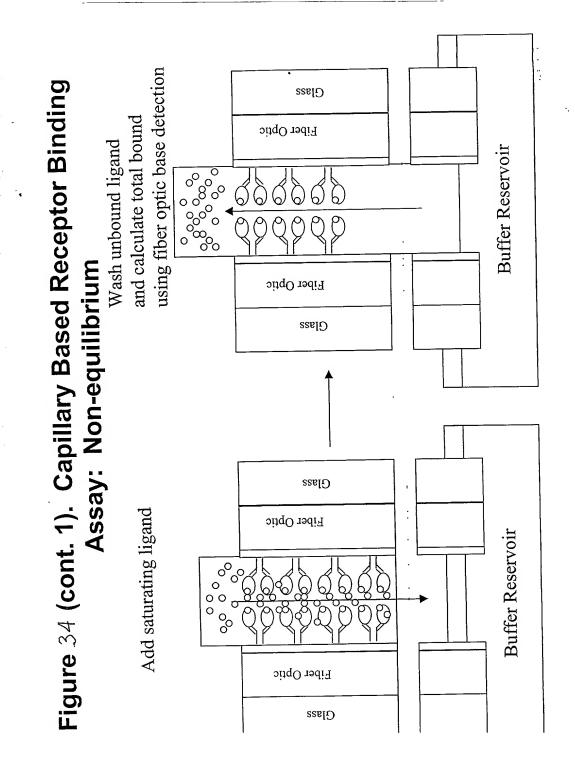


Figure 34 (cont. 2). Capillary Based Receptor Binding Assay: Non-equilibrium

Add compound and use fiber

0 °° 80 optic based detection to observe 0 Glass 0 Fiber Optic 0 kinetics Fiber Optic 0 0 Glass boo 0 00 00 0 00 8 & Consponded Reservoit 0 Glass Fiber Optic compound reservoir Move capillary to Fiber Optic 0 ∞ Glass $p \infty$ 000 80 0 00

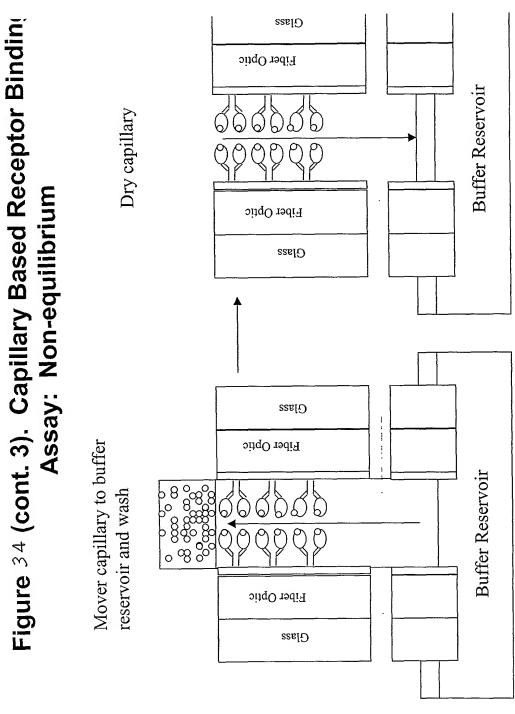
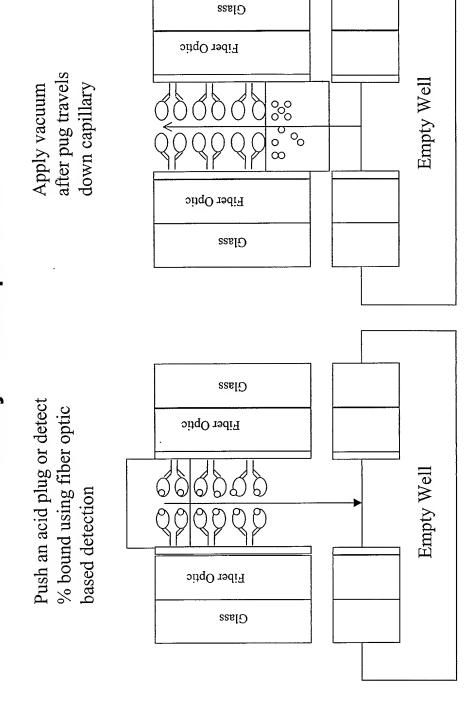
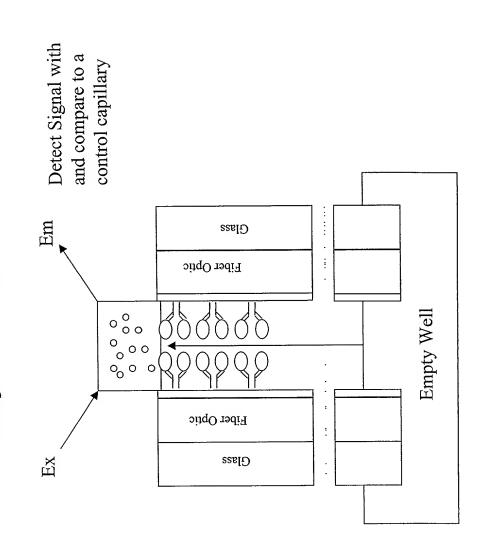


Figure 34 (cont. 4). Capillary Based Receptor Binding Assay: Non-equilibrium



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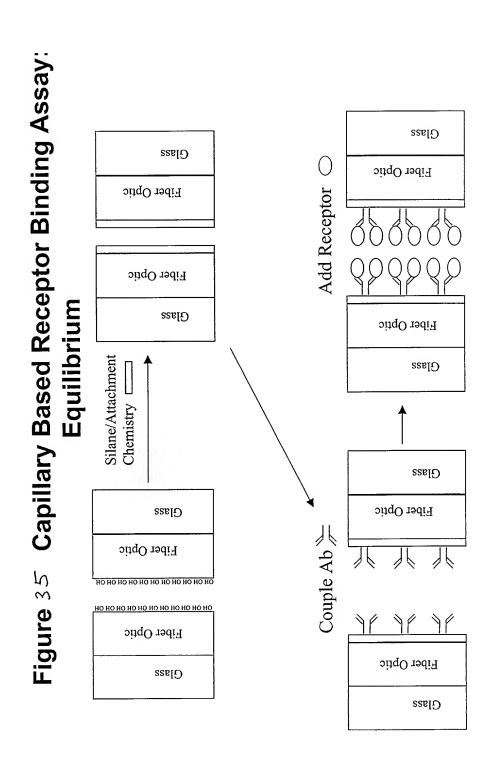


Figure 35 (cont. 1). Capillary Based Receptor Binding Assay: Equilibrium

compound/ligand reservoir. Move Capillary to

Add solution and let system reach equilibrium. Detect equilibrium using fiber optic base detection.

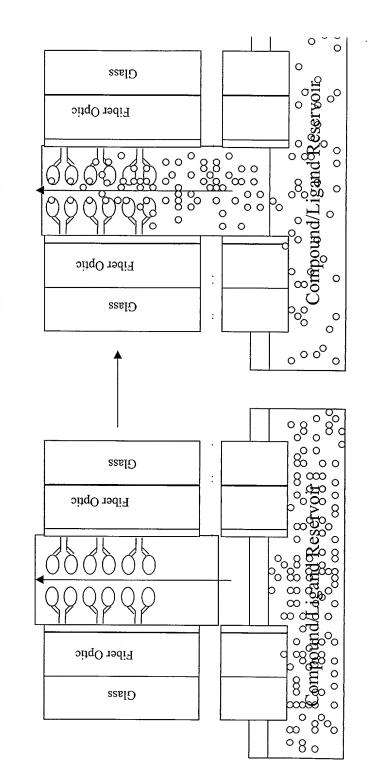


Figure 35 (cont. 2). Capillary Based Receptor Binding

Class Fiber Optic **Buffer Reservoir** Dry Capillary Fiber Optic Assay: Equilibrium Class reservoir and wash capillary with Glass buffer. Detect % bound using fiber optic based detection. Move capillary to a buffer Fiber Optic **Buffer Reservoir** Fiber Optic Glass

Glass

Fiber Optic

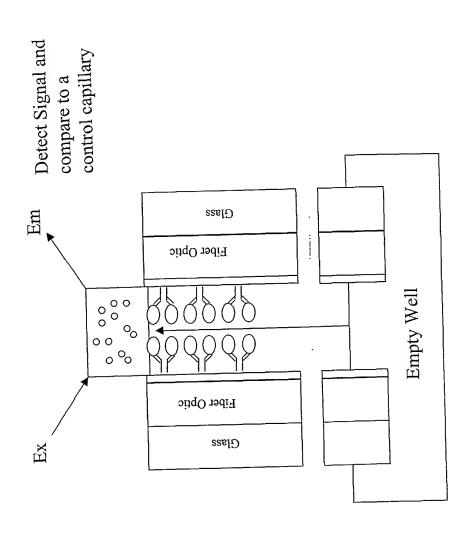
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after pug travels Empty Well down capillary Apply vacuum 000 000 0 Fiber Optic Glass Glass Detect signal using fiber optic base detection or elute bound Fiber Optic Empty Well ligand with acid. Fiber Optic Glass

Figure 35 (cont . 4). Capillary Based Receptor Binding Assay: Equilibrium



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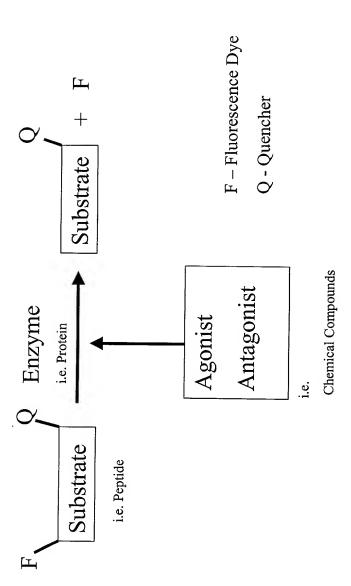


Figure 36

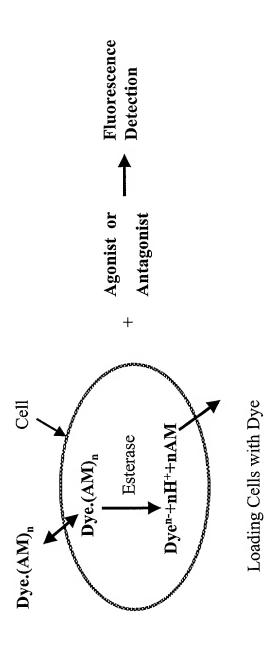


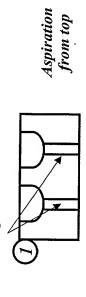
Figure 37

Assay Based on Tracking Cytosolic [Ca++]

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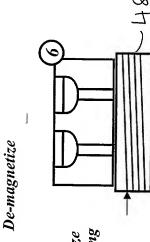
Protein Array & Cell Array

Library of antigen or antibody Attached to magnetic beads





Mixing circle







38A Fla.

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Aspiration from top

Vacuum from bottom

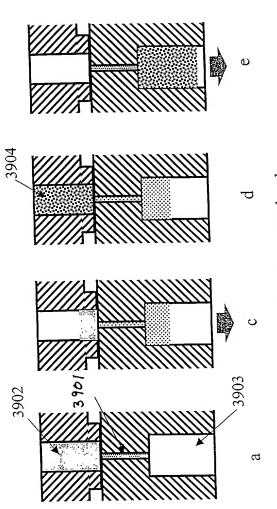
Incubation & Imaging Positive pressure from bottom Aspiration from top Apply assay

Fluid-Array™ XHTS

TODSORY4. UZISOR

FIG. 38B

Fig. ψ_0 Metering with through hole plates and mixing



3902 - reagent A (i.e. enzyme) in through hole plate A 3901 - compound and compound storage chamber

3903 - mixing/reaction chamber

3904 - reagent B (i.e. substrate) in through hole plate B

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Fig. 39 One embodiment of the capillary array cartridge design

